

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a chimeric peptide and comprises a HER-2 B cell epitope, a T helper (Th) epitope, and a linker joining said HER-2 B cell epitope to said Th epitope; wherein the sequence of said HER-2 B cell epitope being from 15 to 40 amino acids in length and comprising a sequence is selected from the group consisting of:

TGTDMLRLPASPETHLDM, SEQ ID NO: ~~NO: 1~~, or a functional equivalent thereof;

TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO: ~~NO: 4~~, or a functional equivalent thereof;

ALVTYNTDTFESMPNPEGRT, SEQ ID NO: ~~NO: 5~~, or a functional equivalent thereof;

PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO: ~~NO: 6~~, or a functional equivalent thereof;

LFRNPHQALLHTANRPEDE, SEQ ID NO: ~~NO: 9~~, or a functional equivalent thereof;

CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO: ~~NO: 10~~, or a functional equivalent thereof; and

KPDLSYMPIWKFPDEEGA, SEQ ID NO: ~~NO: 11~~, or a functional equivalent thereof

wherein the Th epitope comprises a sequence selected from the group consisting of:

N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO: 13;

P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO: 14;

Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO: 15;

F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO: 16;

L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO: 17;

F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO: 18; and

T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO: 19; and

wherein the linker consists of from one to 15 amino acids.

2. canceled

3. (Currently Amended) The composition of claim 1, wherein the sequence of the HER 2-B is SEQ ID NO: 6 ~~wherein the Th epitope is a promiscuous Th epitope of from 14 to 22 amino acids in length, and wherein said linker is from 1 to 15 amino acids in length.~~

4. (Currently Amended) The composition of claim 1, wherein the Th epitope comprises a sequence selected from the group consisting of the following sequence:

~~N S V D D A L I N S T I Y S Y F P S V, SEQ. ID. NO. 13, or a functional equivalent thereof; ———~~

~~P G I N G K A I H L V N N Q S S E, SEQ ID NO. 14, or a functional equivalent thereof;~~

~~Q Y I K A N S K F I G I T E L, SEQ ID NO. 15, or a functional equivalent thereof;~~

~~F N N F T V S F W L R V P K V S A S H L E, SEQ ID NO. 16, or a functional equivalent thereof;~~

~~L S E I K G V I V H R L E G V, SEQ ID NO. NO: 17, or a functional equivalent thereof;~~

~~F F L L T R I L T I P Q S L N, SEQ ID NO. 18, or a functional equivalent thereof; and~~

~~T C G V G V R V R S R V N A A N K K P E, SEQ ID NO. 19, or a functional equivalent thereof.~~

5. (previously presented) The composition of claim 1 wherein the linker comprises the sequence GPSL, SEQ ID NO. 20.

6. (Currently Amended) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a multivalent peptide and comprises 2 or more HER-2 B cell epitopes, a Th cell epitope, and a template;

wherein each of said 2 or more HER-2 B cell epitopes are different from the others , and wherein the sequence of each of said 2 or more HER-2 B cell epitopes is ~~from 15 to 40 amino acids in length and comprises a sequence~~ selected from the group consisting of:

~~TGTDMLRLPASPETHLDM, SEQ ID NO. NO: 1, or a functional equivalent thereof;~~

~~AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;~~

~~LWKDIFHKNNQLALTLDITNRS, SEQ ID NO. 3, or a functional equivalent thereof;~~

~~TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO. NO: 4, or a functional equivalent thereof;~~

~~ALVTYNTDTFESMPNPEGRYT, SEQ ID NO. 5, or a functional equivalent thereof;~~
~~PLHNQEVTAEADGTQRAEKCSKPCA, SEQ ID NO. NO: 6, or a functional equivalent thereof;~~
~~PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;~~
~~LYISAWPDSLPLDSVFNQLQ, SEQ ID NO. 8, or a functional equivalent thereof;~~
~~LFRNP HQALLHTANRPEDE, SEQ ID NO. NO: 9, or a functional equivalent thereof;~~
~~CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof;~~
~~KPDLSYMPIWKFPDEEGA, SEQ ID NO. NO: 11, or a functional equivalent thereof; and~~
~~INGTHSCVDLDDKGC PAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and~~
~~INGTHSCVDLDDKGC PAEQR, SEQ ID NO. NO: 42,~~

wherein the Th epitope comprises a sequence selected from the group consisting of:
N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO: 13;
P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO: 14;
Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO: 15;
F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO: 16;
L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO: 17;
F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO: 18; and
T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO: 19;
wherein the HER-2 B cell epitopes and the Th cell epitope are attached to the template, and
wherein the template comprises two strands of alternating leucine and lysine residues connected
by a linker consisting of one to 15 amino acids .

7. (Currently Amended) The composition of claim 6, wherein the sequence of one of the 2 or more HER-2 B cell epitopes is SEQ ID NO: 6, and wherein the sequence of another of the 2 or more HER-2 B cell epitopes is SEQ ID NO: 42 ~~wherein said template is a core β sheet.~~

8. (Currently Amended) The composition of claim 7, wherein the sequence of the Th epitope is SEQ ID NO: 17 ~~wherein the core β sheet comprises two strands of alternating leucine and lysine residues connected by a linker.~~

9-20 canceled

21. (withdrawn/currently amended) A method of stimulating an immune response in a subject comprising administering to said subject a ~~composition selected from the group consisting of the composition of claim 1, the composition of claim 9, and a polypeptide which comprises the composition of claim 1 and the composition of claim 9~~ chimeric peptide that comprises a HER-2 B cell epitope, a T helper (Th) epitope, and a linker joining said HER-2 B cell epitope to said Th epitope; wherein the sequence of said HER-2 B cell epitope is selected from the group consisting of:

TGTDMLRLPASPETHLDM, SEQ ID NO. 1;

TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO: 4;

PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO: 6;

LFRNPHQALLHTANRPEDE, SEQ ID NO: 9, and

KPDLSYMPIWKFPDEEGA, SEQ ID NO: 11;

wherein the Th epitope comprises a sequence selected from the group consisting of:

N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO: 13;

P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO: 14;

Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO: 15;

F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO: 16;

L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO: 17;

F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO: 18; and

T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO: 19; and

wherein the linker consists of from one to 15 amino acids

22. (withdrawn/currently amended) A method of stimulating a an immune response in a subject, comprising: administering a multivalent peptide to said subject; wherein said multivalent peptide comprises:

(a) 2 or more HER-2 B cell epitopes, a Th cell epitope, and a template, wherein each of said two or more HER-2 B cell epitopes are different from the others , and wherein said HER-2 B cell epitopes and said Th cell epitope are attached to said template, ~~or~~

(b) ~~2 or more HER-2 CTL epitopes, a Th cell epitope, and a template, wherein said two or more HER-2 CTL epitopes are different, and wherein said HER-2 CTL epitopes and said Th cell epitope are attached to said template, or~~

(e) ~~one or more HER-2 B cell epitopes, one or more HER-2 CTL epitope, a Th cell epitope, and a template, wherein said one or more HER-2 B cell epitopes, said one or more HER-2 CTL epitopes and said Th cell epitope are attached to said template;~~

wherein the sequence of each of said 2 or more HER-2 B cell epitopes comprises a sequence is selected from the group consisting of:

~~TGTDMLRLPASPETHLDM, SEQ ID NO. NO: 1, or a functional equivalent thereof;~~
~~AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, or a functional equivalent thereof;~~
~~LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, or a functional equivalent thereof;~~
~~TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO. NO: 4, or a functional equivalent thereof;~~
~~ALVTYNTDTFESMPNPEGRT, SEQ ID NO. 5, or a functional equivalent thereof;~~
~~PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. NO: 6, or a functional equivalent thereof;~~
~~PESFDGDPASNTAPLQPE, SEQ ID NO. 7, or a functional equivalent thereof;~~
~~LYISAWPDSLPLDSVFQNLQ, SEQ ID NO. 8, or a functional equivalent thereof;~~
~~LFRNP HQALLHTANRPEDE, SEQ ID NO. NO: 9, or a functional equivalent thereof;~~
~~CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof;~~
~~KPDLSYMPIWKFPDEEGA, SEQ ID NO. NO: 11, or a functional equivalent thereof; and~~
~~INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and~~
INGTHSCVDLDDKGCPAEQR, SEQ ID NO: 42,

wherein the Th epitope comprises a sequence selected from the group consisting of:

N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO: 13;
P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO: 14;
Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO: 15;
F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO: 16;
L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO: 17;
F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO: 18; and
T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO: 19;

wherein the HER-2 B cell epitopes and the Th cell epitope are attached to the template, and
wherein the template comprises two strands of alternating leucine and lysine residues connected
by a linker consisting of one to 15 amino acids

and

~~wherein each of said HER-2 CTL epitopes comprises a sequence selected from the group consisting of:~~

~~ILWKDIFHK, SEQ ID. NO. 21; or a functional equivalent thereof;
ILKETELRK, SEQ ID. NO. 22; or a functional equivalent thereof;
VLRENTSPK, SEQ ID. NO. 23; or a functional equivalent thereof;
AARPAGATL, SEQ ID. NO. 24; or a functional equivalent thereof;
LPASPETHL, SEQ ID. NO. 25; or a functional equivalent thereof;
LPTHDPSP, SEQ ID. NO. 26; or a functional equivalent thereof;
CRWGLLLAL, SEQ ID. NO. 27; or a functional equivalent thereof;
RRFTHQSDV, SEQ ID. NO. 28; or a functional equivalent thereof;
GRILHNGAY, SEQ ID. NO. 29; or a functional equivalent thereof;
TYLPTNASL, SEQ ID. NO. 30; or a functional equivalent thereof;
EYVNARHCL, SEQ ID. NO. 31; or a functional equivalent thereof;
AYSLTLQGL, SEQ ID. NO. 32; or a functional equivalent thereof;
ALCRWGLLL, SEQ ID. NO. 33; or a functional equivalent thereof;
HLYQGCQV, SEQ ID. NO. 34; or a functional equivalent thereof;
QLRSLTEIL, SEQ ID. NO. 35; or a functional equivalent thereof;
ILHNGAYSL, SEQ ID. NO. 36; or a functional equivalent thereof;
ILLVVVLGV, SEQ ID. NO. 37; or a functional equivalent thereof;
DLTSTVQLV, SEQ ID. NO. 38; or a functional equivalent thereof;
VLVKSPNHV, SEQ ID. NO. 39; or a functional equivalent thereof;
KIFGSLAFL, SEQ ID. NO. 40; or a functional equivalent thereof; and
HSAVVGIL, SEQ ID. NO. 41; or a functional equivalent thereof.~~

23. (canceled)

24. (canceled)

25. (withdrawn /currently amended) A method of treating cancer in a subject comprising administering a pharmaceutical composition to said subject, said pharmaceutical composition comprising:

~~the composition of claim 1 or the composition of claim 9, and~~
a pharmaceutically acceptable vehicle, and
a chimeric peptide that comprises a HER-2 B cell epitope, a T helper (Th) epitope, and a linker joining said HER-2 B cell epitope to said Th epitope; wherein the sequence of said HER-2 B cell epitope is selected from the group consisting of:

TGTDMLRLPASPETHLDM, SEQ ID NO. 1;
TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO: 4;
PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO: 6;
LFRNPHQALLHTANRPEDE; SEQ ID NO: 9, and
KPDLSYMPIWKFPDEEGA, SEQ ID NO: 11;

wherein the Th epitope comprises a sequence selected from the group consisting of:
N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO: 13;
P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO: 14;
Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO: 15;
F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO: 16;
L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO: 17;
F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO: 18; and
T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO: 19; and
wherein the linker consists of from one to 15 amino acids

26. (withdrawn/currently amended) The method of claim 25, wherein the subject is a human and has one of the following cancers or a predisposition to one of the following cancers: breast cancer, ovarian cancer, lung cancer, prostate cancer, and colon cancer.

27. (withdrawn/currently amended) The method of claim 25, wherein the ~~vehicle is biodegradable and is selected from the group consisting of an emulsion comprising a pharmaceutically acceptable oil/water emulsion and a biodegradable microsphere or nanosphere comprising a polylactide-polyglycolic acid polymer~~ the sequence of the HER-2 B cell epitope is SEQ ID NO: 6.

28. (withdrawn/currently amended) The method of claim 27, wherein the ~~oil is squalene or squalane~~ the Th epitope comprises SEQ ID NO: 17 and the linker comprises SEQ ID NO: 20.

29. (withdrawn/currently amended) The method of claim 27, wherein the ~~microsphere is from 0.1 to 50 nanometers in diameter and comprises poly (D, L lactide-co-glycide)~~ cancer is breast cancer.

30. (canceled)

31. (withdrawn / currently amended) The multivalent peptide of claim 6, wherein the sequence of one of said 2 or more multivalent peptide comprises a HER-2 B cell epitopes which comprises is ~~INGTHSCVDLDDKGCPAEQR, SEQ ID NO. 42 or a functional equivalent thereof,~~ wherein the sequence of another of said two or more a-HER-2 B cell epitopes which comprises is SEQ ID NO. 6 or a functional equivalent thereof, and wherein the sequence of another of said two or more a HER-2 B cell epitopes is which comprises SEQ ID NO. 9 or a functional equivalent thereof.

32. (withdrawn/currently amended) A method of treating a subject with cancer comprising administering a mixture of chimeric peptides to the subject, wherein said mixture comprises 2 or more chimeric peptides, wherein each of said 2 or more chimeric peptides comprise a HER-2 B cell epitope, a T helper (Th) epitope; and a linker joining said HER-2 B cell epitope to said Th epitope; wherein the HER-2 B cell epitope of each of said 2 or more chimeric peptides are different from the others , and ~~comprise a sequence~~ wherein the sequence of each of said HER-2 B cell epitopes is selected from the group consisting of:

TGTDMLRLPASPETHLDM, SEQ ID NO. ~~NO:~~ 1, ~~or a functional equivalent thereof;~~

AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO. 2, ~~or a functional equivalent thereof;~~

LWKDIFHKNNQLALTLIDTNRS, SEQ ID NO. 3, ~~or a functional equivalent thereof;~~

TLIDTNRSRACHPCSPMCKGSRGWGESSEDCQSLT, SEQ ID NO. ~~NO:~~ 4, ~~or a functional equivalent thereof;~~

ALVTYNTDTFESMPNPEGRT, SEQ ID NO. 5, ~~or a functional equivalent thereof;~~

PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO. ~~NO:~~ 6, ~~or a functional equivalent thereof;~~

PESFDGDPASNTAPLQPE, SEQ ID NO. 7, ~~or a functional equivalent thereof;~~

~~LYISAWPDSLPLDSVFNQLQ, SEQ ID NO. 8, or a functional equivalent thereof;~~
~~LFRNPHQALLHTANRPEDE, SEQ ID NO. NO: 9, or a functional equivalent thereof;~~
~~CLPCHPECQPQNGSVTCFGPEADQCVACAHYKDP, SEQ ID NO. 10, or a functional equivalent thereof;~~
~~KPDLSYMPIWKFPDEEGA, SEQ ID NO. NO: 11, or a functional equivalent thereof; and~~
~~INGTHSCVDLDDKGCPAEQRAS, SEQ ID NO. 12, or a functional equivalent thereof; and~~
~~INGTHSCVDLDDKGCPAEQR, SEQ ID NO. NO: 42,~~

wherein the Th epitope comprises a sequence selected from the group consisting of:
N-S-V-D-D-A-L-I-N-S-T-I-Y-S-Y-F-P-S-V, SEQ. ID. NO: 13;
P-G-I-N-G-K-A-I-H-L-V-N-N-Q-S-S-E, SEQ ID NO: 14;
Q-Y-I-K-A-N-S-K-F-I-G-I-T-E-L, SEQ ID NO: 15;
F-N-N-F-T-V-S-F-W-L-R-V-P-K-V-S-A-S-H-L-E, SEQ ID NO: 16;
L-S-E-I-K-G-V-I-V-H-R-L-E-G-V, SEQ ID NO: 17;
F-F-L-L-T-R-I-L-T-I-P-Q-S-L-N, SEQ ID NO: 18; and
T-C-G-V-G-V-R-V-R-S-R-V-N-A-A-N-K-K-P-E, SEQ ID NO: 19; and
wherein the linker consists of from one to 15 amino acids.

33. (withdrawn /currently amended) The method of claim 32 wherein the subject is treated with a chimeric peptide comprising a HER-2 B cell epitope ~~which comprises whose sequence is~~ SEQ ID NO. NO: 42 ~~or a functional equivalent thereof,~~ a chimeric peptide comprising a HER-2 B cell epitope ~~which comprises whose sequence is~~ SEQ ID NO. NO: 6 ~~or a functional equivalent thereof,~~ and a chimeric peptide comprising a HER-2 B cell epitope ~~which comprises whose sequence is~~ SEQ ID NO. NO: 9 ~~or a functional equivalent thereof.~~

34. (new) The composition of claim 6, wherein the linker comprises SEQ ID NO: 20.

35. (new) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a chimeric peptide and comprises a HER-2 B cell epitope, a T helper (Th) epitope, and a linker joining said HER-2 B cell epitope to said Th epitope; wherein SEQ ID NO:

6 is the sequence of the HER 2-B cell epitope, wherein SEQ ID NO: 17 is the sequence of the Th epitope, and wherein SEQ ID NO: 20 is the sequence of the linker.

36. (New) A composition for stimulating an immune response to HER-2 protein, wherein said composition is a multivalent peptide and comprises 2 or more HER-2 B cell epitopes, a Th cell epitope, and a template;

wherein each of said 2 or more HER-2 B cell epitopes are different from the others, and wherein the sequence of one of the 2 or more HER-2-B cell epitopes is SEQ ID NO: 6, and wherein the sequence of another of said 2 or more HER-2 B cell epitopes is SEQ ID NO: 42, wherein the Th epitope comprises SEQ ID NO:17; wherein the HER-2 B cell epitopes and the Th cell epitope are attached to the template; and wherein the template comprises two strands of alternating leucine and lysine residues connected by a linker consisting of one to 15 amino acids.

37. (New) The method of claim 36 wherein the linker comprises SEQ ID NO:20.

38. (New) The method of claim 32, wherein the sequence of the HER-2 B cell epitope of one of the chimeric peptides is SEQ ID NO: 6, and wherein the sequence of the HER-2 B cell epitope of another of the chimeric peptides is SEQ ID NO: 42.

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